BIOGRAPHICAL SKETCH

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NAME: Verzi, Michael Paul

eRA COMMONS USERNAME (credential, e.g., agency login): MVERZI01

POSITION TITLE: Professor, Rutgers, the State University of New Jersey

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
The College of New Jersey	B.A.	05/ 2000	Biology, Chemistry
University of California, San Francisco	Ph.D.	03/2006	Molecular Biology
Dana-Farber Cancer Inst, Harvard Medical School	Postdoc	2006-2011	Gastrointestinal Development

A. Personal Statement

My entire career has revolved around my fascination with transcriptional regulatory mechanisms and *in vivo* genetic approaches, from my Ph.D. with Brian Black at UCSF, studying transcriptional regulation of cardiac and craniofacial development using mouse genetics[1], to my postdoctoral training with Ramesh Shivdasani at Dana Farber Cancer Institute developing whole-genome approaches to study transcriptional regulation and epigenetics in gastrointestinal biology[2]. Our work on the transcriptional mechanisms of colon cancer led us to a surprising finding that oncogenic mutations of *BRAF* trigger cell differentiation rather than tumorigenesis. We then found multiple genetic modifiers that create a permissive environment to *BRAF*-driven tumorigenesis[3-4]. My lab at Rutgers focuses on discovering the transcriptional regulatory mechanisms that drive intestinal development, homeostasis, and colorectal cancer[3-4]. I have recently been appointed the Faculty Director of the Organoid Development Shared Resource which is in development at Rutgers Cancer Institute of New Jersey.

Citations:

1. **Verzi MP**, Shin H, He HH, Sulahian R, Meyer CA, Montgomery RK, Fleet JC, Brown M, Liu XS, Shivdasani RA. Differentiation-specific histone modifications reveal dynamic chromatin interactions and partners for the intestinal transcription factor CDX2. Dev Cell. 2010 Nov 16;19(5):713-26. doi: 10.1016/j.devcel.2010.10.006. Erratum in: Dev Cell. 2014 Dec 22;31(6):801. PMID: 21074721; PMCID: PMC3001591.
2. Chen L, Toke NH, Luo S, Vasoya RP, Fullem RL, Parthasarathy A, Perekatt AO, **Verzi MP**. A reinforcing HNF4-SMAD4 feed-forward module stabilizes enterocyte identity. Nat Genet. 2019 May;51(5):777-785. doi: 10.1038/s41588-019-0384-0. Epub 2019 Apr 15. PMID: 30988513; PMCID: PMC6650150.
3. Tong K, Pellón-Cárdenas O, Sirihorachai VR, Warder BN, Kothari OA, Perekatt AO, Fokas EE, Fullem RL, Zhou A, Thackray JK, Tran H, Zhang L, Xing J, Verzi **MP**. Degree of Tissue Differentiation Dictates Susceptibility to BRAF-Driven Colorectal Cancer. Cell Rep. 2017 Dec 26;21(13):3833-3845. doi: 10.1016/j.celrep.2017.11.104. PMID: 29281831; PMCID: PMC5747303.
4. Tong K, Kothari OA, Haro KS, Panda A, Bandari MM, Carrick JN, Hur JJ, Zhang L, Chan CS, Xing J, Gatza ML, Ganesan S, **Verzi MP**. SMAD4 is critical in suppression of BRAF-V600E serrated tumorigenesis. Oncogene. 2021 Oct;40(41):6034-6048. doi: 10.1038/s41388-021-01997-x. Epub 2021 Aug 27. PMID: 34453124; PMCID: PMC8559887.

B. Positions and Honors

Positions and Employment

- Professor, Rutgers, The State University of New Jersey 2022 - present
- Associate Professor, Rutgers, The State University of New Jersey 2017 - 2022
- Assistant Professor, Rutgers, The State University of New Jersey 2011 – 2017

Honors and Services

- Rutgers Board of Trustees Award for Excellence in Research 2022
- NIH NIDDK Study Section member DDK-C 2020 - present
- AGA member, Councilor to GDCH section 2017-present
- Department of Defense, Grant Reviewer, Colon Cancer I-II 2017-2018
- NIH ZRG1 DKUS-D (90) Study Section (ad hoc) 2019
- NIH NIDDK Study Section ZDK1 GRB-7 2018-2019
- Fellow of the Crohn's & Colitis Foundation of America (CCFA) 2007-2010
- F32 Postdoctoral Fellowship award from NIH (declined to accept CCFA)
- American Cancer Society Postdoctoral Fellowship (declined to accept CCFA)
- Young IBD Investigator Award, Crohn's & Colitis Foundation of America 2010
- 2014 American Cancer Society Scholar Grant (declined to accept NCI R01)
- 2014 DoD CDMRP award for Colon Cancer (declined to accept NCI R01)
- Howard Hughes Medical Institute Predoctoral Fellowship 2001- 2005
- National Science Foundation Predoctoral Fellowship 2001 (declined for HHMI)
- Barry M. Goldwater National Scholarship 1999-Spring 2000

C. Contributions to Science

1. **Elucidating regulatory mechanisms of Colon Cancer**: The primary interest of our lab is to identify transcriptional regulatory mechanisms of normal gastrointestinal function and contrast them with disease states, primarily colon cancer. A recent focus area for us has been in Serrated tumor formation driven by BRAF (a-c). As a postdoc, I applied my findings about transcription factor binding to help understand why genetic variation in an enhancer of *MYC* could lead to elevated expression levels and cancer risk by altering the binding strength of the transcription factor to the enhancer.

    a. Tong K, Pellón-Cárdenas O, Sirihorachai VR, Warder BN, Kothari OA, Perekatt AO, Fokas EE, Fullem RL, Zhou A, Thackray JK, Tran H, Zhang L, Xing J, **Verzi MP**. Degree of Tissue Differentiation Dictates Susceptibility to BRAF-Driven Colorectal Cancer. Cell Reports. 2017 Dec 26;21(13):3833-3845.
    b. Perekatt AO, Shah PP, Cheung S, Jariwala N, Wu A, Gandhi V, Kumar N, Feng Q, Patel N, Chen L, Joshi S, Zhou A, Taketo MM, Xing J, White E, Gao N, Gatza ML, **Verzi MP**. SMAD4 Suppresses WNT-Driven Dedifferentiation and Oncogenesis in the Differentiated Gut Epithelium. Cancer Res. 2018 Sep 1;78(17):4878-4890.
    c. Tong K, Kothari OA, Haro KS, Panda A, Bandari MM, Carrick JN, Hur JJ, Zhang L, Chan CS, Xing J, Gatza ML, Ganesan S, **Verzi MP**. SMAD4 is critical in suppression of BRAF-V600E serrated tumorigenesis. Oncogene. 2021 Oct;40(41):6034-6048. doi: 10.1038/s41388-021-01997-x. Epub 2021 Aug 27.
    d. Pomerantz MM, Ahmadiyeh N, Jia L, Herman P**, Verzi MP**, Doddapaneni H, Beckwith CA, Chan JA, Hills A, Davis M, Yao K, Kehoe SM, Lenz HJ, Haiman CA, Yan C, Henderson BE, Frenkel B, Barretina J, Bass A, Tabernero J, Baselga J, Regan MM, Manak JR, Shivdasani R, Coetzee GA, Freedman ML. The 8q24 cancer risk variant rs6983267 shows long-range interaction with MYC in colorectal cancer. Nature Genetics. 2009 Aug;41(8):882-4.

2. **Bringing epigenomics to the GI community**: I was among the first to use epigenomic approaches to characterize gastrointestinal processes. In two key papers, we showed how chromatin structure and transcription factor binding events were related to gastrointestinal gene expression. We were able to predict, and then subsequently demonstrate, that multiprotein transcriptional regulatory complexes

underlie condition-specific gene expression in the intestinal epithelium. This work laid the foundation for epigenomic interrogation on normal intestinal homeostasis and led to our subsequent body of work, partially detailed below. We extended our initial characterization of the intestinal epithelial epigenome to probe more specific questions of intestinal stem cell function and intestinal lineage decisions. We validated these approaches using compound mutant mice, and thus added a functional component to the epigenomic analysis that increases the tangible value of these studies.

a. Kim TH, Li F, Ferreiro-Neira I, Ho LL, Luyten A, Nalapareddy K, Long H, **Verzi MP**, Shivdasani R, An epigenetic basis for lateral inhibition and cell plasticity in intestinal differentiation. Nature. Jan 12, 2014. PMC4151315.
b. **Verzi MP**, Shin H, He HH, Sulahian R, Meyer CA, Montgomery RK, Fleet JC, Brown M, Liu XS, Shivdasani RA. Differentiation-specific histone modifications reveal dynamic chromatin interactions and partners for the intestinal transcription factor CDX2. Dev Cell. 2010 Nov 16;19(5):713-26. PMC3001591
c. **Verzi MP**, Hatzis P, Sulahian R, Philips J, Schuijers J, Shin H, Freed E, Lynch JP, Dang DT, Brown M, Clevers H, Liu XS, Shivdasani RA. TCF4 and CDX2, major transcription factors for intestinal function, converge on the same cis-regulatory regions. Proc Natl Acad Sci U S A. 2010 Aug 24;107(34):15157-62. PMC2930576
d. **Verzi MP**, Shin H, Ho LL, Liu XS, Shivdasani RA. Essential and redundant functions of caudal family proteins in activating adult intestinal genes. Mol Cell Biol. 2011 May;31(10):2026-39.

3. **Defining how Transcription Factor Regulatory Complexes control Intestinal homeostasis**: We have previously studied HNF4A due to it being a top hit in epigenomic screens to identify transcriptional effectors of the response to colon inflammation or normal intestinal differentiation. We subsequently described a series of transcriptional functions of HNF4A.

a. Chen L, Toke NH, Luo S, Vasoya RP, Fullem RL, Parthasarathy A, Perekatt AO, **Verzi MP**. A reinforcing HNF4-SMAD4 feed-forward module stabilizes enterocyte identity. Nat Genet. 2019 May;51(5):777-785. doi: 10.1038/s41588-019-0384-0. Epub 2019 Apr 15. PMID: 30988513; PMCID: PMC6650150.
b. Chen L, Cao W, Aita R, Aldea D, Flores J, Gao N, Bonder EM, Ellison CE, **Verzi MP**. Three-dimensional interactions between enhancers and promoters during intestinal differentiation depend upon HNF4. Cell Rep. 2021 Jan 26;34(4):108679. doi: 10.1016/j.celrep.2020.108679. PMID: 33503426; PMCID: PMC7899294.
c. Chen L, Luo S, Dupre A, Vasoya RP, Parthasarathy A, Aita R, Malhotra R, Hur J, Toke NH, Chiles E, Yang M, Cao W, Flores J, Ellison CE, Gao N, Sahota A, Su X, Bonder EM, **Verzi MP**. The nuclear receptor HNF4 drives a brush border gene program conserved across murine intestine, kidney, and embryonic yolk sac. Nat Commun. 2021 May 17;12(1):2886. doi: 10.1038/s41467-021-22761-5. PMID: 34001900; PMCID: PMC8129143.
d. Chen L, Vasoya RP, Toke NH, Parthasarathy A, Luo S, Chiles E, Flores J, Gao N, Bonder EM, Su X, **Verzi MP**. HNF4 Regulates Fatty Acid Oxidation and Is Required for Renewal of Intestinal Stem Cells in Mice. Gastroenterology. 2020 Mar;158(4):985-999.e9. doi: 10.1053/j.gastro.2019.11.031. Epub 2019 Nov 22. PMID: 31759926; PMCID: PMC7062567.

4. **Integration of epigenomics approaches to study developmental systems:** My lab and I have experience in identifying novel developmental phenotypes and have demonstrated that we can hone in on the transcriptional regulatory mechanisms contributing to these phenotypes.

a. Kumar N, Tsai YH, Chen L, Zhou A, Banerjee KK, Saxena M, Huang S, Toke NH, Xing J, Shivdasani RA, Spence JR, **Verzi MP**. The lineage-specific transcription factor CDX2 navigates dynamic chromatin to control distinct stages of intestine development. Development. 2019 Mar 1;146(5):dev172189. doi: 10.1242/dev.172189. PMID: 30745430; PMCID: PMC6432663.
b. Kumar N, Srivillibhuthur M, Joshi S, Walton KD, Zhou A, Faller WJ, Perekatt AO, Sansom OJ, Gumucio DL, Xing J, Bonder EM, Gao N, White E, **Verzi MP**. A YY1-dependent increase in aerobic metabolism is indispensable for intestinal organogenesis. Development. 2016 Oct 15;143(20):3711-3722. doi: 10.1242/dev.137992. PMID: 27802136; PMCID: PMC5087649.

c. Srivillibhuthur M, Warder BN, Toke NH, Shah PP, Feng Q, Gao N, Bonder EM, **Verzi MP**. TFAM is required for maturation of the fetal and adult intestinal epithelium. Dev Biol. 2018 Jul 15;439(2):92-101. doi: 10.1016/j.ydbio.2018.04.015. Epub 2018 Apr 22. PMID: 29684311; PMCID: PMC5978755.
d. Perekatt AO, Valdez MJ, Davila M, Hoffman A, Bonder EM, Gao N, **Verzi MP**. YY1 is indispensable for Lgr5+ intestinal stem cell renewal. Proc Natl Acad Sci U S A. 2014 May 27;111(21):7695-700. doi: 10.1073/pnas.1400128111. Epub 2014 May 12. PMID: 24821761; PMCID: PMC4040551.

5. **Transcription factor biology in development**: My graduate training in the lab of Brian Black at UCSF focused on transcription factor biology of the developing cardiac and neural crest tissues. We probed transcription factor function via enhancer-reporter constructs *in vivo* and validated transcription factor functions with conditional knockout mice. My longstanding interests in how transcription factors control biological processes began at this time and continues.

a. **Verzi MP**, Agarwal P, Brown C, McCulley DJ, Schwarz JJ, Black BL. The transcription factor MEF2C is required for craniofacial development. Dev Cell. 2007 Apr;12(4):645-52. doi: 10.1016/j.devcel.2007.03.007. PMID: 17420000; PMCID: PMC1920108.
b. Verzi MP, Stanfel MN, Moses KA, Kim BM, Zhang Y, Schwartz RJ, Shivdasani RA, Zimmer WE. Role of the homeodomain transcription factor Bapx1 in mouse distal stomach development. Gastroenterology. 2009 May;136(5):1701-10. doi: 10.1053/j.gastro.2009.01.009. Epub 2009 Jan 14. PMID: 19208343; PMCID: PMC2955323.
c. Yu S, Tong K, Zhao Y, Balasubramanian I, Yap GS, Ferraris RP, Bonder EM, Verzi **MP**, Gao N. Paneth Cell Multipotency Induced by Notch Activation following Injury. Cell Stem Cell. 2018 Jul 5;23(1):46-59.e5. doi: 10.1016/j.stem.2018.05.002. Epub 2018 Jun 7. PMID: 29887318; PMCID: PMC6035085.
d. Agarwal P, **Verzi MP,** Nguyen T, Hu J, Ehlers ML, McCulley DJ, Xu SM, Dodou E, Anderson JP, Wei ML, Black BL. The MADS box transcription factor MEF2C regulates melanocyte development and is a direct transcriptional target and partner of SOX10. Development. 2011 Jun;138(12):2555-65. doi: 10.1242/dev.056804. PMID: 21610032; PMCID: PMC3100711.

A full list of Dr. Verzi's publications can be found at:
https://www.ncbi.nlm.nih.gov/sites/myncbi/michael.verzi.1/bibliography/40704327/public/?sort=date&direction=descending